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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

RAWLINGS, STEPHEN L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/13/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/556,833

Applicant(s)

CURRY ET AL.

Examiner

Stephen L. Rawlings, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-21 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. The amendment filed on April 12, 2002 in Paper No. 13 is acknowledged and has been entered. Claims 1-3, 5-7, and 11 have been amended.
2. Claims 1-21 are pending in the application. Claims 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.
3. Claims 1-16 are currently under prosecution.

Grounds of Objection and Rejection Withdrawn

4. Unless specifically reiterated in this Office Action, the grounds of objection and rejection set forth in the previous Office Action are withdrawn.

Grounds of Objection Maintained

5. As stated in the Office Action mailed November 6, 2001 (Paper No. 11), the disclosure was objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code, which are impermissible and require deletion.

The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding incorporation by reference.

In reply to the Office Action Applicants have attempted to comply with requirement by amending the specification to inactivate the hyperlinks by deleting "http://" from the text. In addition, Applicants have submitted, "there is no attempt to incorporate essential material into the instant application by reference to a hyperlink or other form of browser-executable code" (page 5, paragraph 2).

In response to Applicant's remark, references to websites are still made in the specification, despite deletion of "http://" from the text to inactivate the associated hyperlinks. Although Applicants have clearly stated that the references to the websites are not attempts to incorporate essential material into the specification, it is not clear whether Applicants are attempting to incorporate non-essential information by inclusion of the references to the websites.

MPEP 608.01(p) does not provide for incorporation of essential or non-essential material by reference to hyperlinks or other forms of browser-executable code. Essential subject matter may only be incorporated by reference to (1) US patents and pending US applications, or patents or other publications published by a foreign country or a regional patent office, (2) non-patent publications, (3) a US patent or application which itself incorporates material by reference, or (4) a foreign application. Non-essential information may be incorporated by reference to (1) patents or applications published by the United States, or patents or other publications published by a foreign country or a regional patent office, (2) prior filed, commonly owned US applications, (3) non-patent publications.

It is impermissible that a patent's disclosure incorporate essential or non-essential material by reference to embedded hyperlinks and/or other forms of browser-executable code, because the information contained in the websites or databases to which the hyperlinks or other forms of browser-executable code connect may not be maintained on the Internet for the duration of the patent's term and may not contain the same information after the filing date of an application that was contained in the website or database on or before the filing date of the application. Since the information contained in a website may vary, it is not evident that information contained in a website will always remain useful to the practitioner or even applicable to the invention; and information contained in an extinct website cannot possibly be helpful to the practitioner. Furthermore, the validity of a patent containing a reference to a hyperlink or other form of browser-executable code may be reasonably questioned if the website(s) to which the hyperlink(s) connect were relied upon by the patentee(s) to provide sufficient disclosure or description of the invention to meet the requirements of 35 USC § 112,

first and second paragraphs. As such, although some patents have issued, which contain references to hyperlinks or other forms of browser-executable code, recitation of such references is not permitted and the presence of such references in any US patent merely suggests an oversight by Applicant and/or Examiner. Otherwise, a hyperlink or other form of browser-executable code may be permitted if the hyperlink or other form of browser-executable code is part of the claimed invention, but in this case, the Office would disable the hyperlink or other form of browser-executable code.

In general, if the Applicant expects to rely upon the information contained in the websites or databases to provide antecedent basis for the subject matter of claims in a parent application or related applications, and if the material is properly incorporated by reference in the referencing application, Applicant would be required to amend the specification of the referencing application to include the material incorporated by reference to the website at the hyperlink or other forms of browser-executable code, or other non-permissible sources and to provide a declaration by Applicant or Applicant's representative stating that the amendatory material consists of the same material incorporated by the reference originally. See MPEP § 608.01(p).

In the instant application, the specification refers to widely used, publicly available gene and protein sequence databases and other resources. Applicants are reminded that it is not necessary to disclose that which is widely known in the art.

As to the question of new matter, since it cannot be determined whether or how the information content of the website(s) or database(s) to which the hyperlinks or other forms of browser-executable code connect has changed since the filing date of the application, the introduction of any information gleaned from the websites or databases into the specification would in fact appear to violate the written description requirement of 35 USC § 112, first paragraph. The deletion of the hyperlinks or other forms of browser-executable code from the specification does not constitute new matter, although if Applicant is presently relying upon the information content of such websites or databases to provide support for language in the claims, which does not appear adequately supported by the actual text of the specification, as filed, then, indeed such claim language also would appear to be new matter. In short, since the content of the

websites or databases on the date the application was filed cannot be ascertained, the information that was contained in the websites will not be considered part of the original disclosure.

Thus, regardless of whether or not Applicant complies with the requirement to delete references to websites, Applicant should not expect to be able to rely upon information present only in the website to establish a priority date for related applications filed after this application.

Grounds of Claim Rejections Maintained and Reply to Applicants' Remarks

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in the previous Office Action mailed November 6, 2001 (Paper No. 11).

(a) Claims 1-16 are indefinite because claims 1, 2, and 3 recite the phrase "effective amounts". The phrase "effective amounts" is indefinite when the claims fail to state the functions that are to be achieved. See *In re Frederiksen & Nielsen*, 213 F 2d 547, 102 USPQ 35 (CCPA 1954). Accordingly, one of ordinary skill in the art is not reasonably apprised of the metes and bounds of the invention.

(b) Claims 1-16 are indefinite because claims 1, 2, and 3 recite the phrase "irradiating said subject with light absorbed by said photosensitizer". Recitation of the phrase renders the claims indefinite because it is unclear how light, which is absorbed by a photosensitizer, can be used to irradiate a subject. Accordingly, one of ordinary skill in the art is not reasonably apprised of the metes and bounds of the invention. Amending the claims to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention can obviate this rejection.

(c) Claims 1-16 are indefinite because claims 1 and 3 fail to recite a positive process step that clearly relates back to the preamble of the claims. Accordingly, one of ordinary skill in the art is not reasonably apprised of the metes and bounds of the invention.

(d) Claims 1, 2, and 4-16 are vague and indefinite because claims 1 and 2 recite the term "metastatic tumors". Recitation of the term renders the claim vague and indefinite because it cannot be ascertained from the claim or from the disclosure whether the term is meant to refer to any tumor with metastatic potential or any metastasis (i.e., a secondary tumor that has developed by the spreading of tumor cells from a primary point of origin to a distant anatomical site). Accordingly, one of ordinary skill in the art is not reasonably apprised of the metes and bounds of the invention.

(e) Claims 2, 4-7 and 10-15 are indefinite because claim 2 recites the phrase "a subject at risk for developing metastatic tumors". Recitation of the phrase renders the claim indefinite because it is unclear to whom the claim refers, because the requisite degree of risk is not defined by the claim or the specification. Moreover, the specification does not provide a standard for ascertaining whether or when a subject is "at risk" and is also void of guidance indicating how one can determine or know when a subject is "at risk". Accordingly, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(f) Claim 15 is vague and indefinite because the claim recites the term "improves". The term "improves" is a relative term that renders the claim indefinite, because the term is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

(g) Claim 15 is vague and indefinite because the claim recites the phrase "with light of a wavelength which improves penetration of the absorbed light". Recitation of the phrase renders the claim vague and indefinite because it is unclear to into what matter the claim requires the irradiation to improve penetration. It is also unclear to what absorbed light the claim requires an improvement in penetration. Furthermore, it is noted that neither the claim nor the specification disclose to what wavelength of light,

which when used to irradiate the undisclosed subject matter improves the penetration of the "absorbed light", the claim refers. Accordingly, one of ordinary skill in the art is not reasonably apprised of the metes and bounds of the invention.

In reply to the previous Office Action, Applicants have traversed these grounds of rejection under 35 USC § 112, second paragraph, arguing:

(a) The methods encompassed by the claims are directed to the effective treatment, prevention, or inhibition of various tumors, and as such, the scope of the subject matter that Applicants regard as their invention would be clear to the ordinary artisan. Nevertheless, the use of the alternative phrasing in the present claims obviates this ground of rejection.

(b) It is accepted in the art to generically refer to irradiation of a part of a subject as "irradiating a subject". Irradiation of a subject as a whole simply activates photosensitizers at locations where photosensitizer is present in the subject's body; therefore no ambiguity is introduced by the phrase.

(c) No basis is offered in the previous Office Action for the asserted requirement for a positive process step that clearly relates back to the preamble of the claim. Nevertheless, recitation of the phrase "wherein said method is photochemical mediated photodynamic therapy (PDT) mediated treatment of said subject" in the present claims obviates this ground of rejection.

(d) The specification is clearly directed to the treatment of metastatic tumors as opposed to pre-metastatic tumors. Furthermore, "[t]he nature of invention as encompassed by claim 2 is that any tumor cells with metastatic potential that have migrated away from the one or more pre-metastatic tumor may be targeted by the disclosed methods and prevented or inhibited from developing into a metastatic tumor" (page 7, paragraph 3). Thus, the term "metastatic tumor" is broad, but not ambiguous. In addition, although the Examiner's reference to the Korbelyk, et al is not understood, there is no indication that the actual tumor used by Korbelyk, et al is metastatic under their conditions.

(e) The basis of this ground of rejection is misplaced. The instant rejection lacks adequate support for asserting that such artisans would not be able to ascertain

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the "requisite degree of risk" since the skilled artisan is fully capable of determining when a risk of metastatic tumor development is present.

(f) The ability to prevent spurious absorption of a particular wavelength of light is the very act of improving penetration of the light, and this would be understood by the skilled artisan. Because a broad range of improvement in penetration is within the scope of the claim, this ground of rejection is misplaced.

(g) It would be quite clear to the skilled artisan that the improvement to which claim 15 refers is an improvement in penetration of the subject's cells and tissues; what else would it relate to? In addition, it would be clear to the skilled artisan that the light absorbed by the photosensitizer is the absorbed light to which the claim refers and which is thereby required to have improved penetration; what else would it be? Furthermore, the wavelength of light that improves penetration of the wavelength of light absorbed by the photosensitizer is well known in the art or determinable without undue experimentation.

In response to Applicants' arguments:

(a) Contrary to Applicants' remark, the present claims recite the term "effective amounts" without explicitly stating the function or functions that are to be achieved by administering these amounts of the green porphyrin photosensitizer and the immunoadjuvant. Although Applicants have amended the claims to recite, for example, the phrase "for treating metastatic tumors upon irradiation with light absorbed by said photosensitizer", recitation of this phrase does not obviate this ground of rejection because the phrase is merely a recitation of intended use and therefore is not limiting. Moreover, it is still unclear, after the subject is irradiated with light of wavelength absorbed by the photosensitizer, what effect administering the amounts of the photosensitizer and immunoadjuvant to which the claims refer must have. Accordingly, the subject matter that Applicants regard as their invention is not clearly delineated, since the artisan of ordinary skill in the art could not recognize the metes and bounds of the invention because it is unclear what effect or effects must be achieved in practicing the invention. Depending upon the subject matter that Applicants actually regard as their invention, amending claims 1-3 to recite, for example, the

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phrase "administering to a subject [...] effective amounts of a green porphyrin photosensitizer and an immunoadjuvant to elicit an antitumor immune response in the patient" might obviate this ground of rejection.

(b) Contrary to Applicants' remarks, recitation of the phrase introduces ambiguity into the claims for the reason stated in the previous Office Action, and therefore the artisan of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Amending claims 1-3 to recite, for example, the phrase "irradiating said subject with light of a wavelength that is absorbed by the photosensitizer" can obviate this ground of rejection.

(c) Contrary to Applicants' remarks, a basis for this ground of rejection was offered, namely that since claims 1 and 3 fail to recite a positive process step that clearly relates back to the preamble of the claims, the claims fail to particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and therefore the artisan of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. The reason that such an omission renders the claims vague and indefinite is that in the absence of a positive process step that clearly relates back to the preamble of a claim, it is unclear whether each and every step that Applicants regard as essential to the successful practice of the invention, and thereby essential to the fulfillment of the objective stated in the preamble of the claim, is recited in the body of the claim. Recitation of the phrase "wherein said method is photochemical mediated photodynamic therapy (PDT) mediated treatment of said subject" is merely a recitation of alternative terminology used to define the invention and is not a positive process step. Moreover, the definition of the method as "photochemical mediated photodynamic therapy (PDT) mediated treatment of said subject" is not limiting and does not clearly indicate that each and every step that Applicants regard as essential to the successful practice of the invention is recited in the claims. Again, amending claims 1 and 3 to recite, for example, the phrase "whereby said subject is treated", or alternatively "thereby treating said subject" at the end of the present claims can obviate this ground of rejection, and such an amendment will not alter the scope of the claims.

(d) As stated in the previous Office Action, recitation of the term "metastatic tumor" renders claims 1 and 2 vague and indefinite because it cannot be ascertained from the claims or from the disclosure whether the term is meant to refer to any tumor with metastatic potential or any metastasis (i.e., a secondary tumor that has developed by the spreading of tumor cells from a primary point of origin to a distant anatomical site). Applicants previous remarks, which were set forth in Paper No. 6, befuddled the record, since EMT6 is a transplantable metastatic tumor, and yet Applicants asserted that the metastatic tumors to which the claims refer are somehow different from EMT6. Applicants recent remarks suggest that they regard the invention as a method for treating a subject having metastases of a primary tumor, though not necessarily a subject having metastatic cancer. Applicants have stated that the specification is clearly directed to the treatment of metastatic tumors, as opposed to pre-metastatic tumors, and also that the claims are drawn to methods for treating a subject having any disseminated tumor cells with metastatic potential, but it is unclear how the invention can be used to achieve the objective stated in the preamble of claim 2, namely preventing or inhibiting the development of metastatic tumors, i.e., the dissemination of a tumor cell with metastatic potential that has migrated away from the one or more pre-metastatic tumors in the subject, after the fact. In addition, it is not clear what distinguishing characteristics Applicants regard "metastatic" and "pre-metastatic" tumors to have, since the tumor cells that Applicants have contended are to be treated using the claimed method are generally disseminated from a metastatic tumor, not a pre-metastatic tumor. For these reasons contrary to Applicants' assertion, the term "metastatic tumor" is not merely broad, but indefinite. It is unclear whether Applicants regard their invention as a method for treating primary metastatic tumors, not pre-metastatic tumors, or only for treating secondary tumors arising from disseminated micrometastatic disease. Accordingly, the claims do not particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

(e) Although the skilled artisan is capable of determining whether or not a patient is more or less at risk for developing metastatic tumors, every patient is relatively at risk. The issue at hand is the degree to which the subject is required to be at risk for

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developing metastatic tumors. The requisite degree of risk is not clearly delineated by the claims and accordingly the claims do not particularly point out and distinctly claim the subject matter that Applicants regard as their invention. Moreover, the skilled artisan cannot know the metes and bounds of the subject matter that Applicants regard as their invention unless said metes and bounds are clearly delineated by the claims.

(f) Claim 15 requires that additional irradiation improve the penetration of light absorbed without clearly defining the degree to which it is required to do so. While the additional irradiation may in fact improve penetration of light of the wavelength absorbed by the photosensitizer, unless the claims state the requisite degree to which the additional irradiation must improve penetration, or unless the specification provides a standard for ascertaining the requisite degree, the claims are indefinite. In view of Applicants' remarks, perhaps amending claim 15 to recite, for example, "with light of a wavelength that prevents spurious absorption of a subsequent wavelength", rather than "with light of a wavelength which improves penetration of the absorbed wavelength" can obviate this ground of rejection; however, Applicants are cautioned against the introduction of new matter.

(g) Claim 15 is vague and indefinite for the reasons stated in the previous Office Action; Applicants' arguments are acknowledged, but have not been found persuasive. In addition, the question of whether additional, undue experimentation would first be required of the practitioner to have a reasonable expectation of success in practicing the claimed invention is not pertinent to this ground of rejection.

Accordingly, Applicants' arguments have been carefully considered but have not been found persuasive. Therefore, the rejection of claims 1-16 under 35 USC § 112, second paragraph for the reasons set forth in the previous Office Action is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

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at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,290,712-B1 in view of US Patent Nos. 4,436,727-A, 4,912,094-A, 5,149,527-A, 5,579,554-A, 5,770,619-A, 5,929,105-A, 5,990,149-A, 6,071,944-A, and 6,071,944-A for the reasons set forth in the previous Office Action mailed November 6, 2001 (Paper No. 11).

Applicants have traversed these grounds of rejection under 35 USC § 103(a) arguing that the previous Office Action failed to present a *prima facie* case for the obviousness of the claimed invention for the following reasons:

(a) The artisan of ordinary skill would not have had a reasonable expectation of successfully practicing the claimed invention. More particularly, there would have not have been an expectation that green porphyrins could be effective in relation to metastatic tumors. Without such expectation in the art, the use of the cited references in combination to support the obviousness of the invention would require the Examiner's use of impermissible hindsight. In addition, the cited references do not even use the term "metastasis" or any derivative thereof, nor do any of the patents make reference to secondary tumors.

(b) There is no indication of the functional equivalence of the effects mediated by practice of the methods disclosed in the cited references and those mediated by the methods claimed in this application. More particularly, the prior art does not provide any indication or suggestion that photothermal-based effects of practicing the methods of the prior art may be substituted with the singlet oxygen-based effects of practicing presently claimed methods. In addition, the artisan of ordinary skill would not have recognized that a green porphyrin might be substituted into the methods of the prior art to have a reasonable expectation of successfully treating a subject diagnosed with metastatic cancer.

(c) There would have been insufficient motivation to combine the teachings of the prior art to derive the instant invention. The motivation to modify or combine

references must relate to the claimed invention, and the motivation presented in the instant rejection is so broad as to encompass every modification of the methods of the prior art.

In reply to Applicants' arguments,

(a) Applicants have asserted that the artisan of ordinary skill would not have had a reasonable expectation of successfully practicing the claimed invention, or have had a reasonable expectation that green porphyrins could effectively substitute for the photosensitizer used in the methods disclosed by the prior art; however, it is noted that Applicants have not provided any scientific reasoning to support this assertion. Nevertheless, the previous Office Action noted that US Patent No. 6,290,712-B1 ('712) teaches other suitable photosensitizers, which might have reasonably been expected to be equivalent to indocyanine green in effectively inhibiting the growth of malignant tumors, provided that upon absorption of a particular wavelength of light, these photosensitizers have the ability "to create thermal energy, to evolve singlet oxygen and other active molecules, or to be toxic in their own right" (column 7, lines 40-43). The other references cited as the basis of this rejection provide additional reasons that green porphyrins, in particular might reasonably have been expected to effectively substitute for indocyanine green, and these disclosures were noted in the previous Office Action.

In response to Applicants' argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicants' disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Although Applicants have stated that the cited references do not even use the term "metastasis" or any derivative thereof, nor do any of the patents make reference to secondary tumors, as noted in the previous Office Action, '712 makes reference to

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metastatic cells. In addition, as example of a cited patent that makes reference to secondary tumors, it was noted in the previous Office Action that US Patent No. 5,579,554-A teaches that the cancers can be primary or metastatic. Nevertheless, it is also noted that that some of the features upon which Applicants rely (i.e., secondary tumors, singlet oxygen-based effects) are not recited in the rejected claims. While it is not clear that Applicants' disclosure supports recitation of such limiting features in the claims, Applicants should be aware that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

(b) Applicants second argument is essentially the same as the first; and accordingly, Applicants are referred to the paragraphs above in which a reply to these arguments has already been made.

(c) In response to Applicants' argument that there is no suggestion to combine the references, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, in view of the teachings of US Patents Nos. 4,436,727-A, 4,912,094-A, 5,149,527-A, 5,579,554-A, 5,770,619-A, 5,929,105-A, 5,990,149-A, and 6,071,944-A, one of ordinary skill in the art would have been motivated to improve the method of US Patent No. 6,290,712-B1 because there was a long-felt need at the time for more efficacious therapeutic means for treating, preventing, or inhibiting primary and secondary cancers in humans and other animals. Contrary to Applicants' assertion, the motivation to combine and modify the methods of the prior art, which was found in the prior art and in the knowledge generally available to one of ordinary skill in the art, and which was presented in the rejection, is not so broad as to encompass a motivation to make every modification of the methods of the prior art. Rather the motivation presented in the rejection would only have been sufficient to motivate the artisan to make those modifications that would have been obvious to one of ordinary skill in the art in view of

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the teachings of the prior art and of knowledge generally available to one such artisan. Nevertheless, evidence that such motivation could be found in the art at the time the invention was made is disclosed in US Patent No. 6,290,712-B1 ('712). As noted in the previous Office Action, '712 teaches, "it is an object of this invention to improve the treatment of neoplasms by combining photodynamic and immunologic therapies in such a way as to cause immediate neoplastic cellular destruction while concomitantly stimulating the self-immunological defense system against proliferation of residual or metastatic cells" (column 5, lines 24-29). Thus, it is evident that the artisan of ordinary skill in the art at the time the invention was made was in fact motivated to improve the methods of treatment because there had been a long-felt need at the time for more efficacious therapeutic means for treating, preventing, or inhibiting primary and secondary cancers in humans and other animals.

In addition, Applicants have objected to "the proposition that 'malignant' in reference to a tumor or cancer necessarily indicates invasiveness or metastatic nature in all circumstances" (page 10, paragraph 4). In reply, The On-Line Medical Dictionary (published at the Dept. of Medical Oncology, University of Newcastle upon Tyne © Copyright 1997-2002 - The CancerWEB Project) defines the term "metastatic" as "[s]pread of a disease from the organ or tissue of origin to another part of the body. The dictionary defines "malignant" as "[h]aving the properties of anaplasia, invasion and metastasis, said of tumours". Thus, common definitions of the terms "malignant" and "metastatic" support the assertion that malignant tumors are invasive and metastatic. Additionally, Dictionary.com (Copyright © 2002, Lexico LLC) defines the term "metastatic tumor" as "a tumor that is malignant and tends to spread to other parts of the body [syn: malignant tumor, malignant neoplasm]", which suggests that the terms malignant and metastatic are synonymous.

Accordingly, Applicants' arguments have been carefully considered but have not been found persuasive. Therefore, the rejection of claims 1-16 under 35 USC § 103(a) for the reasons set forth in the previous Office Action is maintained.

New Grounds of Claim Objections

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10. Claim 1 is objected to because of the following informalities:

Claim 1 is objected to because the claim recites the phrase "component derived from" in brackets. In view of the marked-up copy of the claims, it is apparent that Applicants intended to delete this phrase. Appropriate correction is required.

Conclusion

11. No claims are allowed.

12. Applicants' amendment necessitated the new ground of objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Stephen L. Rawlings, Ph.D.

Examiner

Art Unit 1642

slr

August 9, 2002


ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600